

Sleep-dependent neuroplastic changes during auditory perceptual learning



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ABSTRACT

Auditory perceptual learning is accompanied by a significant increase in the amplitude of sensory evoked responses on the second day of training. This is thought to reflect memory consolidation after the first practice session. However, it is unclear whether the changes in sensory evoked responses depend on sleep per se or whether a break between training sessions would sufficiently yield similar changes. To assess the relative contributions of sleep and passage of time (wakefulness) on the sensory evoked responses, we recorded auditory evoked fields using magnetoencephalography while participants performed a vowel segregation task in three different sessions separated by 12 h over two consecutive days. The first two practice sessions were scheduled in the morning and evening of the same day for one group and the evening and morning of subsequent days for the other group. For each participant, we modeled the auditory evoked magnetic field with single dipoles in bilateral superior temporal planes. We then examined the amplitudes and latencies of the resulting source waveforms as a function of sleep and passage of time. In both groups, performance gradually improved with repeated testing. Auditory learning was paralleled by increased sustained field between 250 and 350 ms after sound onset as well as sensory evoked fields around 200 ms after sound onset (i.e., P2m amplitude) for sessions taking place on the same and different days, respectively. These neuromagnetic changes suggest that auditory learning involves a consolidation phase that occurs during the wake state, which is followed by a sleep-dependent consolidation stage indexed by the P2m amplitude.

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1. Introduction

Daily practice sessions have been shown to improve a listener's ability to discriminate sound frequency (Irvine, Martin, Klimkeit, & Smith, 2000), temporal intervals (Wright, Buonomano, Mahncke, & Merzenich, 1997), auditory patterns (Espinoza-Varas & Watson, 1986; Watson, 1980), consonant vowels (McClaskey, Pisoni, & Carrell, 1983; Schwab, Nusbaum, & Pisoni, 1985), and concurrent vowels (Reinke, He, Wang, & Alain, 2003). It has been postulated that cortical plasticity in sensory cortex underlies these training-induced improvements in sound perception (Gilbert, Sigman, & Crist, 2001; Moore, Amitay, & Hawkey, 2003). Animal studies showing that training involving daily practice sessions over a long period of time is associated with changes in the topographical organization

representing the trained sensory attributes (Recanzone, Merzenich, Jenkins, Grajski, & Dinse, 1992; Recanzone, Schreiner, & Merzenich, 1993). These changes in sensory representations may involve the expression of new synaptic connections, thereby resulting in an enlarged cortical representation of a trained stimulus (Recanzone et al., 1993; Rutkowski & Weinberger, 2005). For example, Recanzone et al. (1993) trained non-human primates to make fine pitch discriminations over several daily training sessions and found enlarged cortical maps and sharper receptive field tunings at the trained frequency, which correlated with increased perceptual acuity.

In humans, non-invasive neuroimaging techniques such as electroencephalography (EEG) and magnetoencephalography (MEG) are increasingly used to examine neuroplastic changes that accompany training-induced improvement in listening skills. The auditory evoked potentials (AEPs) and auditory evoked fields (AEFs, the complement to AEP obtained with MEG) are obtained by averaging epochs of brain waves that are time-locked to either external sensory events (e.g., a sound stimulus) or internal events such as

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perception and decision-making processes. Some of these brainwaves are exogenous (i.e., obligatory) and reflect only the physical properties of the external events regardless of the observer's intention and motivation. In contrast, other brainwaves are endogenous because they are determined by psychological factors such as attention and expectation. Importantly, the presence and characteristics of AEPs and AEFs can be quantified during the course of training in terms of latency and amplitude. AEPs and AEFs are comprised of sequences of several positive and negative deflections (i.e., waves). The most prominent sensory responses are the N1 and P2 waves, which related to the detection (Hillyard, Squires, Bauer, & Lindsay, 1971; Martin, Sigal, Kurtzberg, & Stapells, 1997) and perception of sound objects (Alain & Tremblay, 2007), respectively. The conscious discrimination and identification of sounds objects are often associated with a late sustained wave/field peaking between 250 and 800 ms post-stimulus (Alain & Tremblay, 2007).

Early studies assessing the impact of training on brain plasticity compared individuals that differed in terms of their expertise with the material presented. For instance, Shahin, Bosnyak, Trainor, and Roberts (2003) examined the effects of long-term musical training on AEPs and found larger N1c amplitudes (~140 ms) to pure, piano or violin tones in musicians relative to non-musicians. This effect of musical expertise is thought to reflect the activation of the lateral portion of the superior temporal gyrus. In addition, the N1c was accompanied by an enhancement of the P2 (~185 ms) wave (Kuriki, Kanda, & Hirata, 2006; Shahin et al., 2003). A larger N1m (the magnetic counterpart of the electric N1) has also been found for piano tones compared to pure tones in musicians, whereas such difference in N1m was not found in non-musicians (Pantev et al., 1998). Neuromagnetic recordings have also revealed an enhanced N1m that was specific to the principal instrument played by the musician (Pantev, Roberts, Schulz, Engelien, & Ross, 2001).

In addition to cross sectional studies, longitudinal studies that have measured the impact of a training program on auditory evoked responses have also shown shortened N1 latency (Bosnyak, Eaton, & Roberts, 2004; Reinke et al., 2003) as well as an augmentation of N1m amplitude (Menning, Roberts, & Pantev, 2000) after training. The training-related enhancement in N1m may either indicate that more neurons are activated or firing more synchronously. In a more recent study, Tremblay, Shahin, Picton, & Ross (2009) found a significant correlation between performance in voice onset time (VOT) discrimination, expressed in d-prime measures, and pre-training N1 amplitudes, again suggesting an association between N1 measures and learning. Lastly, training has been found to enhance P2 amplitude (Atienza, Cantero, & Dominguez-Marín, 2002; Bosnyak et al., 2004; Reinke et al., 2003; Tremblay, Kraus, McGee, Ponton, & Otis, 2001) after two (Atienza et al., 2002) or three (Bosnyak et al., 2004) daily test sessions.

Interestingly, in the Reinke et al. (2003) study, the P2 enhancement was preceded by rapid neuroplastic changes over the right auditory cortex during the first hour of testing, which occurred only when listeners were attending to the stimuli (Alain, Snyder, He, & Reinke, 2007). Notably, there was no significant increase in P2 amplitude within the first hour of training (Alain et al., 2007). This suggests that the P2 effect indexes a relatively slow learning process that may depend on consolidation taking place during sleep. Sleep plays an important role for the consolidation of newly acquired skills (Bonnet & Arand, 1995; Gaab, Paetzold, Becker, Walker, & Schlaug, 2004; Mednick et al., 2002), and for the automatic detection and orientation of attention to expected deviant stimuli (Atienza, Cantero, & Stickgold, 2004). However, there is also evidence that substantial gains in performance can occur within the same training day as long as individuals are allowed to rest for at least one hour between the two test sessions (Gottselig et al., 2004; Roth, Kishon-Rabin, Hildesheimer, & Karni, 2005).

As mentioned earlier, the training-related increase in P2 amplitude occurs in studies using discrimination tasks after two (Atienza et al., 2002) or three (Bosnyak et al., 2004; Reinke et al., 2003; van Wassenhove & Nagarajan, 2007) daily test sessions, suggesting that it may index a consolidation process that takes place during sleep. However, in those studies the ERP measurements were only taken at the beginning and end of training making it difficult to know whether the changes in P2 amplitude coincide with improvement in performance. This issue was partially addressed in a study by Atienza et al. (2002), who measured ERPs in several test sessions occurring within the same and subsequent days. In the first day, ERPs were recorded in a pre-training session where participants listened passively to sounds that were later presented in the training phase. After a short pause, participants were trained to discriminate the stimuli and were given feedback at the end of each block of trials. Then, the ERPs were recorded immediately after training and 12 h later on the same day. In all ERP recording sessions, participants read a book of their choice (no response required). As expected, the participants' ability to discriminate the stimuli improved with training. Despite behavioral improvement, the N1 and P2 amplitude remained unchanged between the pre-training session and the two post-training sessions taken place during the same day. However, the ERPs recorded on the next day showed a significant increase in P2 amplitude. Notably, this P2 enhancement remained in a subsequent session occurring 12 h later as well as on the following day. The results suggest different time courses for behavioral and neurophysiological indices of learning. The P2 enhancement may reflect consolidation occurring during sleep. However, the study by Atienza et al. (2002) could not establish a direct link between changes in behavioral performance and brain activity because the ERPs were recorded during passive listening. That is, participants ignored the auditory stimuli and read a book of their choosing.

In the present study, performance on a concurrent vowel identification task and auditory evoked fields (AEFs) were compared between three practice sessions across two consecutive days. In one group, neural activity was measured in the morning, evening, and the following morning. In the other group, measurements were taken first in the evening and then in the following morning and evening again (Fig. 1). Such an experimental design allowed us to assess the impact of rest and sleep in the acquisition and consolidation of auditory skills. In addition, we could better determine the relationship between behavioral improvement and training-induced changes in sensory evoked responses. We carried out analyses on source waveforms and also explored the effects of training on oscillatory activity. Brain rhythms are implicated in a wide variety of perceptual and cognitive tasks (especially attention and memory), with different frequency bands playing different roles (Fan et al., 2007). Here, we focused on beta oscillations (13–29 Hz) because it has been shown to be associated with auditory working memory (Peterson & Thaut, 2002; Spitzer & Blankenburg, 2012), and learning (Grossberg, 2013). Furthermore, during an auditory Sternberg task, right temporal beta oscillations increased monotonically with memory load, which were shown to reflect attentional control during short-term memory maintenance and formation of object representations (Leiberg, Kaiser, & Lutzenberger, 2006). Taken together, these studies demonstrated that beta oscillations play an important role in attention and memory. Thus, examining differences in oscillatory data as a function of training could provide new insight into the neural processes involved in auditory learning. The main hypotheses are that (1) changes in behavioral performance and learning-related AEFs correlate with practice, (2) practice-related neuroplastic changes in P2m are greater with sleep (between two consecutive days) than with the passage of time (within the same day), and (3) beta oscillations decreases as the task becomes more automatic.

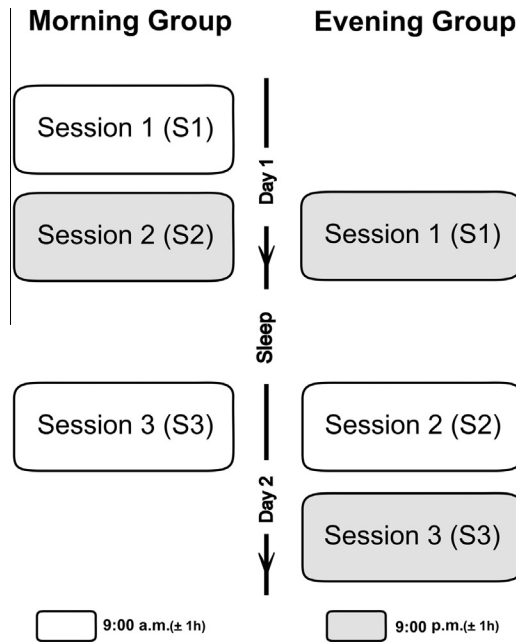


Fig. 1. Experimental paradigm.

2. Materials and methods

2.1. Participants

Twenty-nine volunteers were recruited from the local community and laboratory personnel (Table 1). Informed consent was obtained in written form according to the guidelines established by Baycrest Centre and the University of Toronto. Participants were randomly assigned to a morning ($N = 15$) and an evening ($N = 14$) group. All participants were right-handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), reported English as their first language, had no prior experience with the experimental task, and reported no history of neurological disorders, concussions or hearing loss. Criteria for normal hearing were pure-tone thresholds less than or equal to 25 dB hearing level (HL) for octave frequencies from 250 to 8000 Hz in both ears.

Preference for the time-of-day (TOD) was assessed using the Morningness–Eveningness Questionnaire (MEQ) as shown in Table 2 (Horne & Ostberg, 1976). There were no significant differences in TOD preferences between groups. Sleep quality was subjectively assessed using the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Participants also reported the number of hours of sleep for the night prior to the first ($M = 7$, $SD = 1.46$) and second testing days ($M = 6.79$, $SD = 0.96$). Prior to each session, subjective alertness was assessed

Table 1
Participant characteristics.

Group	Morning		Evening		<i>t</i>	<i>p</i>	95% CI_{diff}
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>			
Age	23.93	3.9	23.07	3.45	.62	.54	−3.68, 1.95
Education	16.27	2.12	16.21	2.49	.06	.95	−1.81, 1.70
EHI	75.56	31.09	78.45	23.83	.27	.79	−18.98, 24.76
MEQ	49.40	7.95	49.64	8.07	.08	.94	−5.87, 6.35
PSQI	6.87	1.60	7.21	1.85	.54	.60	−.97, 1.66

Note: Participant's characteristics did not differ significantly between groups. Level of education included years of primary, secondary, and post-secondary schooling. Edinburgh Handedness Inventory, EHI; Morningness Eveningness Questionnaire, MEQ; Pittsburgh Sleep Quality Index, PSQI; Pittsburgh Sleep Quality Index. CI_{diff} = confidence interval of difference.

Table 2

Frequencies of time of day preference as assessed by the MEQ in each group.

MEQ	Group			
	Morning		Evening	
	<i>F</i>	%	<i>F</i>	%
Definitely evening	0	0	1	7
Moderately evening	4	27	0	0
Neutral	9	60	11	79
Moderately morning	2	13	2	14

using the Stanford Sleepiness test (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973; Kimura, Widmann, & Schroger, 2010). Mixed model ANOVAs showed neither an effect of 'session' ($F_s \leq 1$) nor a 'group' \times 'session' interaction ($F_s \leq 2.94$) for sleep duration and subjective alertness.

2.2. Stimuli and task

All test sessions were carried out in a quiet, magnetically shielded room. The auditory stimuli included four synthetic steady-state American English vowels: "AH" as in /a/, "ER" as in /ɜ/, "EE" as in /i/ and "OO" as in /u/ (Alain, Reinke, He, Wang, & Lobaugh, 2005; Assmann & Summerfield, 1994). Each vowel was 200 ms in duration (2442 samples at a 12.21 kHz sample rate, 16-bit quantization), with fundamental (f_0) and formant frequencies held constant for the entire duration. Onsets and offsets were shaped by two halves of an 8-ms Kaiser window. Double-vowel stimuli were created by combining pairs of phonetically different vowels. In each pair, one vowel was set at a f_0 of 100 Hz while the other vowel was set at 0, 0.25, 0.5, 1, 2, or 4 semitones higher (i.e., 100, 101, 103, 106, 112, or 126 Hz). This arrangement yielded 36 different pairs of vowels. In each session, five blocks of 144 randomized trials (1 block = 36 vowel pairs \times 4 repetitions) were presented with an inter-stimulus interval of 1500 ms. Vowel stimuli were converted to analog form using a real-time processor (RP2; Tucker-Davis Technologies, Inc., Alachua, FL) under the control of a custom MATLAB program (Version 5.3; The Mathworks, Natick, MA) on a Pentium-4 computer (Windows NT), and routed to a headphone driver (HB7; Tucker-Davis Technologies, Inc., Alachua, FL). Binaural stimuli were presented at 60 dB sensation level (SL) through foam insert earphones that were connected by length matched plastic tubes (diameter: 5 mm, length: 1.5 m) to transducers (ER3A; Etymotic Research, Inc., Elk Grove Village, IL). Prior to each session, auditory thresholds were assessed separately for each ear using sample double-vowel stimuli taken from the experimental set.

All participants completed three test sessions over two consecutive days. Each session lasted about one hour (h) and was scheduled either in the morning at 9 a.m. (range: ± 1 h) or in the evening at 9 p.m. (range: ± 1 h). Participants in the morning group partook in the first (S1) and the second (S2) sessions in the morning and evening of the first day and completed the third session (S3) in the morning of the second day. In contrast, participants in the evening group completed S1 in the evening of the first day and S2 and S3 in the morning and evening of the second day. The time between consecutive sessions was about 11 h (± 2 h).

In each session, participants were asked to identify both vowels for each trial. Responses were made with the dominant right hand by sequentially pressing two of four buttons labeled "AH", "ER", "EE" and "OO" for the vowels /a/, /ɜ/, /i/ and /u/, respectively. Prior to each session, vowels were presented individually (24 trials = 4 vowels \times 6 repetitions) and identified by participants via button press. All participants were able to achieve an accuracy of 95% or better in identifying individual vowels. Both vowel tasks were self-paced and no feedback on performance was given.

2.3. Data acquisition and analysis

The neuromagnetic activity was recorded continuously (625 Hz sampling rate, 200 Hz lowpass filtering) using an 151-channel axial-gradiometer type whole-head magnetometer (VSM-Medtech Inc., Port Coquitlam, BC, Canada) with detection coils uniformly spaced 31 mm apart on a helmet-shaped array. Participants sat in an upright position and were fitted with three coils on the nasion and on the left and right pre-auricular points. This allowed co-registration of the head position relative to the MEG sensor at the beginning and end of each recording block. Participants' head shape and coil positions were recorded with a 3-dimensional digitization system (Polhemus Fastrak; Polhemus Inc., Colchester, VT).

For all recording sessions, preprocessing of the data involved applying environmental noise reduction (3rd order gradient balancing) and a power line notch filter at 60 Hz. For eye-blink and heart beat artifact removal, components larger than 2 pT were subtracted from the MEG data prior to averaging using principal component elimination method (Kobayashi & Kuriki, 1999). The analysis epoch included 600 ms of pre- and 1400 ms of post-stimulus activity.

Individual dipole analysis was performed on the grand averaged data (including all stimuli within the session) for each session separately using CTF software. First, the symmetrical dipoles were seeded in the temporal lobe near Heschl's gyrus and then the location and orientation of each dipole were fitted to account for a 32 ms interval centered on the peak of the N1m wave. For each participant, separate dipole solutions were derived for each session using the grand average auditory evoked fields for that session. On average, the resulting source model yielded a residual variance of 15%. In the present study, the source location of the P2m wave could not be identified accurately due to a sustained field that was superimposed on the P2m response. Therefore, we estimated the P2m from the N1m source modeling. Although the N1m and P2m generators may differ slightly in location, the source waveforms from the N1m model yield a reliable estimate of the P2m (Ross & Tremblay, 2009), and does not affect comparisons between experimental sessions and conditions.

The effects of practice on source waveforms were quantified by first computing contrast between sessions. Then, we used permutation tests, as implemented in EEGLAB (statcond.m, 1000 permutations, $p < 0.01$ false discovery rate (FDR, Benjamini, Drai, Elmer, Kafkafi, & Golani, 2001)), to determine the time points over which the difference in source activity between sessions were statistically different.

The proportion of trials in which both vowels were correctly identified, and corresponding response latencies relative to stimulus onset for the first and second button presses (RT_1 and RT_2 , respectively) were analyzed using a mixed model ANOVA with group (two levels: Morning and Evening) as a between-subject variable and session (three levels: S1, S2, S3) as a within-subjects variable. Mean P1m, N1m, and P2m amplitudes were analyzed with the same procedure with a group as a between-subjects factor, and session and hemisphere (two levels) as within-subject factors. Separate one-way ANOVAs were conducted with the Holm-Bonferroni step-down procedure for multiple comparisons (Holm, 1979). When appropriate, the degrees of freedom for effects were adjusted with Greenhouse–Geisser epsilon (ϵ) for sphericity violations. In such cases, the Greenhouse–Geisser adjusted probability estimates and nominal degrees of freedom were reported.

3. Results

3.1. Speech segregation and identification

Participants were trained to segregate and identify two simultaneously presented vowels (randomly chosen from a set of four dif-

ferent vowels, see method). They indicated their responses by sequentially pressing two of the four possible keys on the keyboard (one for each vowel type). Fig. 2 shows the group mean accuracy as a function of the training sessions. As expected, the accuracy of participants at correctly identifying *both* vowels increased with practice ($F(2, 54) = 9.43$, $\eta^2 = .26$; linear trend, $F(1, 27) = 12.48$, $\eta^2 = .32$; $p \leq .005$ in both cases). A main effect of group was not significant ($F(1, 27) = 0.01$, $p = .94$, $\eta^2 = .00$), nor was there any interaction between group and session ($F(2, 54) = 1.55$, $p = .22$, $\eta^2 = .05$; linear trend: $F(1, 27) = 1.37$, $p = .25$, $\eta^2 = .05$). The latter result indicates that the rate of improvement in accuracy was little affected by the training schedule (i.e., morning–evening–morning vs. evening–morning–evening).

In the present study, participants generated two responses on each trial (i.e., they were asked to identify both vowels). Although task instruction did not emphasize speed, we examined the effect of practice on the time needed to generate the first (RT_1) and second (RT_2) responses. The group mean response time for trials in which both vowels were correctly identified is shown for each test session in Fig. 3. For RT_1 , there was a main effect of session ($F(2, 54) = 42.38$, $p < .001$, $\eta^2 = .61$; linear trend: $F(1, 27) = 47.04$, $p < .001$, $\eta^2 = .64$), with participants being quicker at identifying the dominant vowel with practice (pairwise comparison between sessions, $p < .01$ in all cases). The main effect of group was not significant ($F(1, 27) = 0.26$, $p = .61$, $\eta^2 = .01$) nor was the interaction between group and session ($F(2, 54) = 2.66$, $p = .10$, $\eta^2 = .09$; linear trend: $F(1, 27) = 3.20$, $p = .08$, $\eta^2 = .11$). For RT_2 , there was a main effect of session ($F(2, 54) = 50.38$, $p < .001$, $\eta^2 = .65$; linear trend: $F(1, 27) = 57.04$, $p < .001$, $\eta^2 = .68$), with response time decreasing with practice (pairwise comparison between sessions, $p < .001$ in all cases). The main effect of group was not significant ($F(1, 27) = 0.51$, $p = .48$, $\eta^2 = .02$) nor was the interaction between group and session ($F(2, 54) = 0.76$, $p = .47$, $\eta^2 = .03$; linear trend: $F(1, 27) = 0.93$, $p = .34$, $\eta^2 = .03$). Like the accuracy, the results indicate that the rates of improvement in response times were little affected by the training schedule.

3.2. Auditory evoked fields and dipole source location

Fig. 4 shows neuromagnetic data for one representative participant. The AEFs comprised a P1m, N1m, P2m, and slow wave that peaked at about 60, 120, 190, and 500 ms, respectively. The topographic distribution of the N1m amplitude (Fig. 4B) is consistent with generators in auditory cortices along the Sylvian fissure. The dipole source location for a representative participant as well as the group mean location is shown in Fig. 4C. Mean source coordinates were co-registered with the MNI-colin27 template brain and resulted in Talairach coordinates of $x = -49.3$ (right), $y = 24.4$ (posterior), and $z = 0.7$ (superior) in the right and $x = 47.6$, $y = 25.2$, $z = -3.0$ in the left hemisphere. The auditory sources in the right hemisphere were 4.6 mm more anterior than in the left hemisphere ($t(28) = 3.80$, $p < .001$), which is characteristic of the auditory cortices (Penhune, Zatorre, MacDonald, & Evans, 1996) and demonstrates the reliability of the source estimation.

The effects of group and session on N1m source locations were examined by comparing source coordinates (x , y , and z coordinates) separately. For the mediolateral axis, the main effects of group ($F(1, 27) = 0.01$, $p = .96$, $\eta^2 = .00$) and session ($F(2, 54) = 0.76$, $p = .47$, $\eta^2 = .03$) were not significant, nor was the interaction between these two factors ($F(2, 54) = 2.32$, $p = .13$, $\eta^2 = .08$). The N1m was more lateral in the left than in the right hemisphere, $F(1, 27) = 5.28$, $p = .03$, $\eta^2 = .16$. For the anteroposterior axis, there was a main effect of session, $F(2, 54) = 10.38$, $p < .001$, $\eta^2 = .28$). Pairwise comparison revealed that the N1m was more posterior in the third than in the first or second session, $p < .01$ in both cases. There was no difference in N1m source location between the first and second

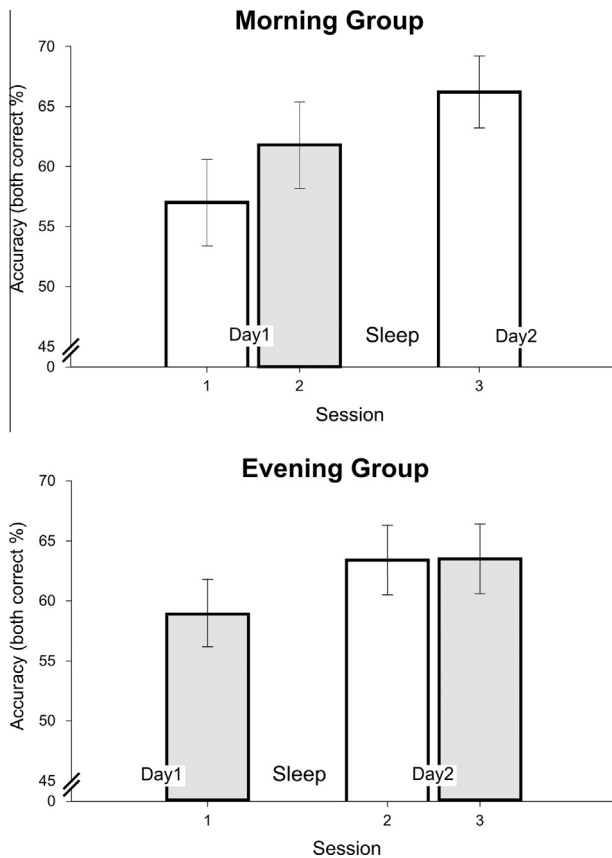


Fig. 2. Mean proportion of trials in which both vowels are accurately identified is shown for each group (A and B) and each participant (C and D). The gradual increase in performance was significant when collapsed across groups, reflecting improvement in participants' ability to process the nondominant vowel. The error bars indicate the standard error of the mean. The Greenhouse–Geisser-adjusted error terms were used for sphericity violations.

sessions. The main effect of group was not significant ($F(1, 27) = 3.98, p = .06, \eta^2 = .13$), nor was the interaction between group and session ($F(2, 54) = 0.33, p = .96, \eta^2 = .00$). For the inferior–superior axis, the main effect of group ($F(1, 27) = 0.01, p = .97, \eta^2 = .00$) and session ($F(2, 54) = 1.26, p = .29, \eta^2 = .04$) were not significant, nor was the interaction between these two factors. The N1m source tended to be superior in the left than in the right hemisphere, but the difference failed to reach significance, $F(1, 27) = 3.93, p = .06, \eta^2 = .13$. No other effect reached statistical significance.

3.3. Source waveforms

For each participant, time series of the AEFs were obtained from single dipoles in bilateral superior temporal planes to examine the effects of sleep and passage of time on the amplitude and latency of the resulting source waveforms. Fig. 5 shows the group mean averaged source waveforms for each session from the left and right auditory cortex. In both groups, the source waveforms comprised a P1m, N1m, and P2m deflection peaking at about 40 ms, 100 ms, and 190 ms after sound onset. There was also a sustained field that peaked at about 500 ms after sound onset. As we predicted, the P2m amplitude increased when the sessions were separated by a night of sleep. That is, only the P2m from the third session showed a marked increase in amplitude for the morning group. In contrast, the P2m from the second and third sessions showed an increase in amplitude for the evening group. For each participant, we calculated a correlation coefficient between accuracy and N1m–P2m peak-to-peak source waveform amplitude from the left and right

hemisphere. The significance of these correlations was then examined through a *t*-test on the group mean correlations. Significant positive correlations were found between N1m and P2m peak-to-peak amplitude and accuracy on the left and right hemispheres, $r = .397$ and $.518$, respectively, $t(28) = 3.16$ and $4.55, p < .005$ in both cases. That is, at the participant level the larger the N1m–P2m amplitude, the greater the improvement in identifying both vowels correctly.

The effects of training schedule on neuromagnetic brain activity are best illustrated by the difference waves between the source waveforms of the three different practice sessions. Confidence limits for the group averages, estimated by bootstrap resampling, confirmed that the difference in P2m amplitude was statistically reliable. For the morning group, confidence bands differed from zero around 200 ms after sound onset between session 1 and session 3 as well as between sessions 2 and 3. However, there was no reliable difference between the morning and evening sessions (sessions 1 and 2). Similarly, for the evening group, confidence bands differed from zero around 200 ms after vowels onset only when the two practice sessions were separated by a night of sleep. In addition to the P2m modulation, we also found enhanced neuromagnetic activity between sessions occurring within the same day. This was characterized by a negative displacement between 250 and 400 ms after sound onset, which was significant only in the right hemisphere (see Figs. 5 and 6). This effect was in the opposite direction for sessions separated by a night of sleep.

3.4. Beta oscillations

In addition to source waveform analysis, we performed a time–frequency analysis of the MEG data. Single trial MEG waveforms were converted into a time–frequency representation using wavelet transform based on the complex Morlet wavelet. This approach complements the analysis of the time domain and allows for the examination of oscillations that occur at various times and frequencies (Bertrand & Tallon-Baudry, 2000; Yuval-Greenberg & Deouell, 2007). We found a decrease in beta (13–29 Hz) power after the stimulus onset, which was followed by a rebound after the response (Fig. 7). The changes in beta power were concentrated around the left central sensors, above the sensorimotor cortices contralateral to the right hand response. Fig. 7C shows the time course of beta event-related desynchronization (ERD) as a function of session in the morning and evening groups. In both groups, the magnitude of beta desynchronization decreased with training. In the time interval between 1200 ms and 1500 ms, corresponding to the group mean RT₁, beta ERD decreased significantly for the morning group between the first and second session on the first day ($t(14) = 4.08, p = .001$) and between the second and third session after a night of sleep ($t(14) = 6.30, p < .001$). In the evening group, beta ERD decreased significantly between the first and the second session, after being separated by a night of sleep ($t(13) = 3.83, p = .002$). However, beta ERD did not show any significant difference between the second and third sessions on the second day ($t(13) = 0.66$).

4. Discussion

Our experimental design allowed us to study the differences between normal activity and sleep on a listener's ability to learn how to identify two vowels presented simultaneously. Training-induced modulation of the P2 amplitudes was the main outcome measure. As expected, participants showed a significant gain in accuracy and shortened response time between the first and second training sessions even when they occurred within the same day. This finding is consistent with auditory perceptual learning

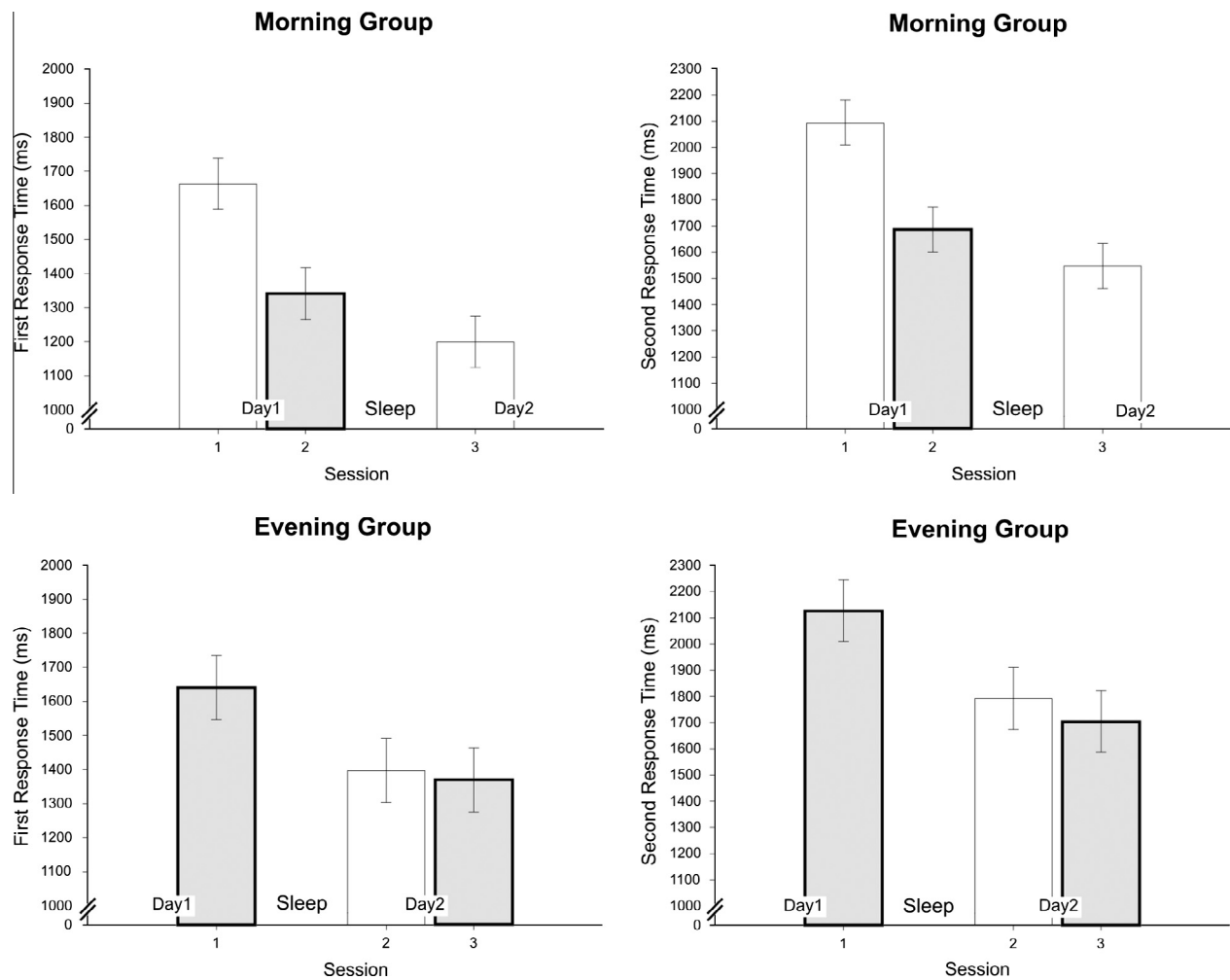


Fig. 3. Group mean response times in accurately identifying both vowels for the first button press (A and B; RT₁) and second button press (C and D; RT₂) as a function of practice. The error bars indicate standard error of the mean. ****p* < .001, ***p* < .01.

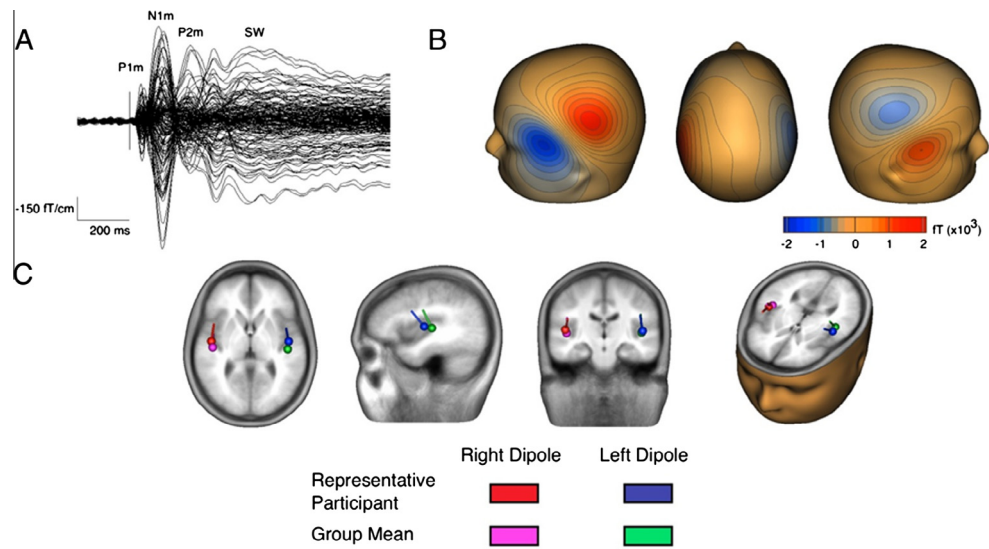


Fig. 4. Neuromagnetic data for one representative participant. (A) AEFs elicited by double-vowel stimuli. (B) Contour maps for the N1m. (C) The dipole location for the N1m with an MRI template from BESA (5.2).

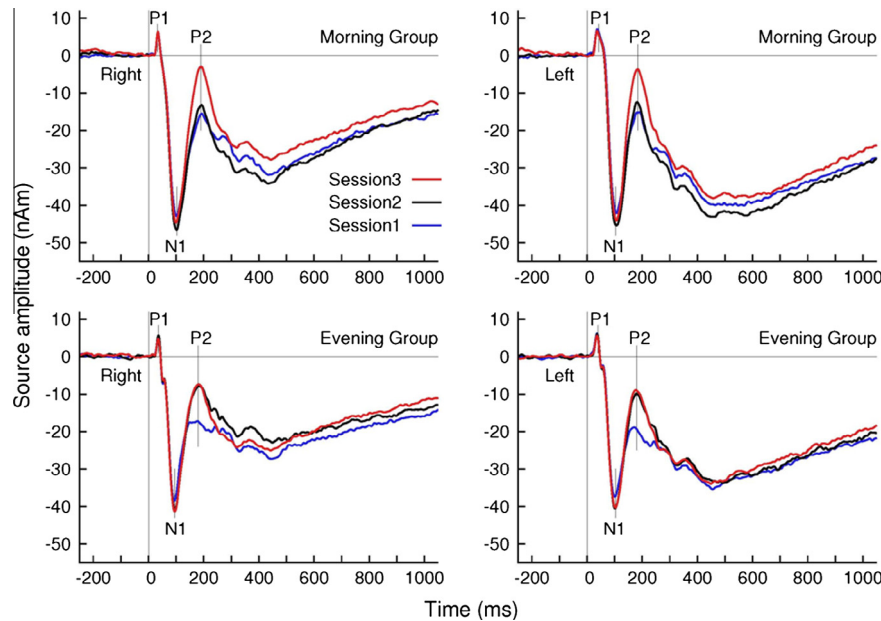


Fig. 5. Group mean averaged source waveforms elicited by concurrent vowel stimuli in the morning group (Top) and evening group (Bottom) for the first (blue), second (black), and third (red) recording sessions.

studies showing improvement in discrimination tasks as long as an hour-long rest is provided between the two sessions (Gottselig et al., 2004; Ortiz & Wright, 2010; Roth et al., 2005). The gain in performance within the same day was associated with changes in sustained field that peaked at about 300 ms after sounds. We also found P2 enhancement, which was present only when the sessions were separated by a night of sleep. At the participant level, the change in N1m–P2m peak-to-peak amplitude correlated with performance, such that greater improvement in accuracy was also associated with larger amplitude. Both behavioral improvement and neurophysiological changes due to practice may reflect a latent memory consolidation taking place after each training session (Ari-Even Roth, Kishon-Rabin, Hildesheimer, & Karni, 2012). The changes in neuroelectric activity between sessions occurring within the same day may reflect early and ongoing consolidation whereas the changes in P2m amplitude could indicate a more long lasting encoding of sensory information into memory during sleep.

At the group level, the neuroplastic changes in P2m amplitude showed a different time course than the behavioral data. While the accuracy and response time of the participants improved between the first and second training sessions independent of sleep, the P2m amplitude increase was greater when the two sessions were separated by a night of sleep rather than the equivalent wakeful rest period. Our findings replicate the results from Atienza et al. (2002) who also observed enhanced P2 amplitude when the two sessions were separated by 24 h (i.e., after a night of sleep) and no reliable change when separated by only 12 h. As participants were given the same amount of time (~12 h) between test sessions in these studies, the current findings cannot be attributed to the passage of time. Furthermore, in the present study, task parameters were identical across all sessions and therefore ruled out the role of differing task exposure. Finally, as the increase in the P2m amplitude depended only on sleep and not on the amount of stimulus learning before sleep (i.e., one or two sessions), any “first session” effects can be ruled out. Since participants had no prior experience with the experimental task, the changes in P2m amplitude may reflect consolidation processes that are distinct to newly acquired information. For participants who were scheduled first in the evening, the P2m enhancement observed the next

morning was maintained into the evening of the same day. Our results suggest that this information requires one night of sleep to materialize and then subsequently persist.

While the current results show a mark P2m amplitude increment after a night of sleep, the behavioral effects did not demonstrate any additional improvement after a night of sleep. This was unexpected in light of earlier research showing the benefit of sleep on sensory discrimination (Atienza et al., 2004; Brawn, Nusbaum, & Margoliash, 2010; Gaab et al., 2004). The reasons for this are unclear, but could be related to the task used in the present study. That is, the double-vowel task is very difficult as it requires the segregation and identification of concurrent speech tokens. These two processing stages are then followed by the stimulus–response mapping in which listeners must compare the incoming speech signals with representation in working memory. One could imagine that the time course of learning may vary between these processes, making it more difficult to detect the benefit of sleep on task performance. In other words, a simpler perceptual or cognitive task may have revealed the benefit of sleep. Further research is needed to explore this possibility.

The time course of learning-related changes in response time and P2m amplitude was also different. That is, the participants’ response times decreased after each session while P2m enhancement was observed only after a night of sleep. Therefore, the P2m enhancement does not appear to index improvement in stimulus–response mapping, response selection and/or execution. A previous study has even observed increased P2 amplitude for stimuli regardless of any overt behavioral responses (Tremblay, Inoue, McClannahan, & Ross, 2010). Hence, the P2 enhancement may reflect neuroplastic changes in stimulus representations associated with repeated exposure and could serve as an index of familiarity with sound objects. Further support for such an interpretation comes from cross sectional studies that have compared musicians and non-musicians. Usually, researchers report larger P2/P2m amplitude in musicians when participants were presented with musical stimuli (Kuriki et al., 2006; Shahin, Roberts, Pantev, Trainor, & Ross, 2005; Shahin et al., 2003). Furthermore, the use-dependent nature of this response is shown by the fact that the larger P2/P2m amplitude is also specific to the sound from the musi-

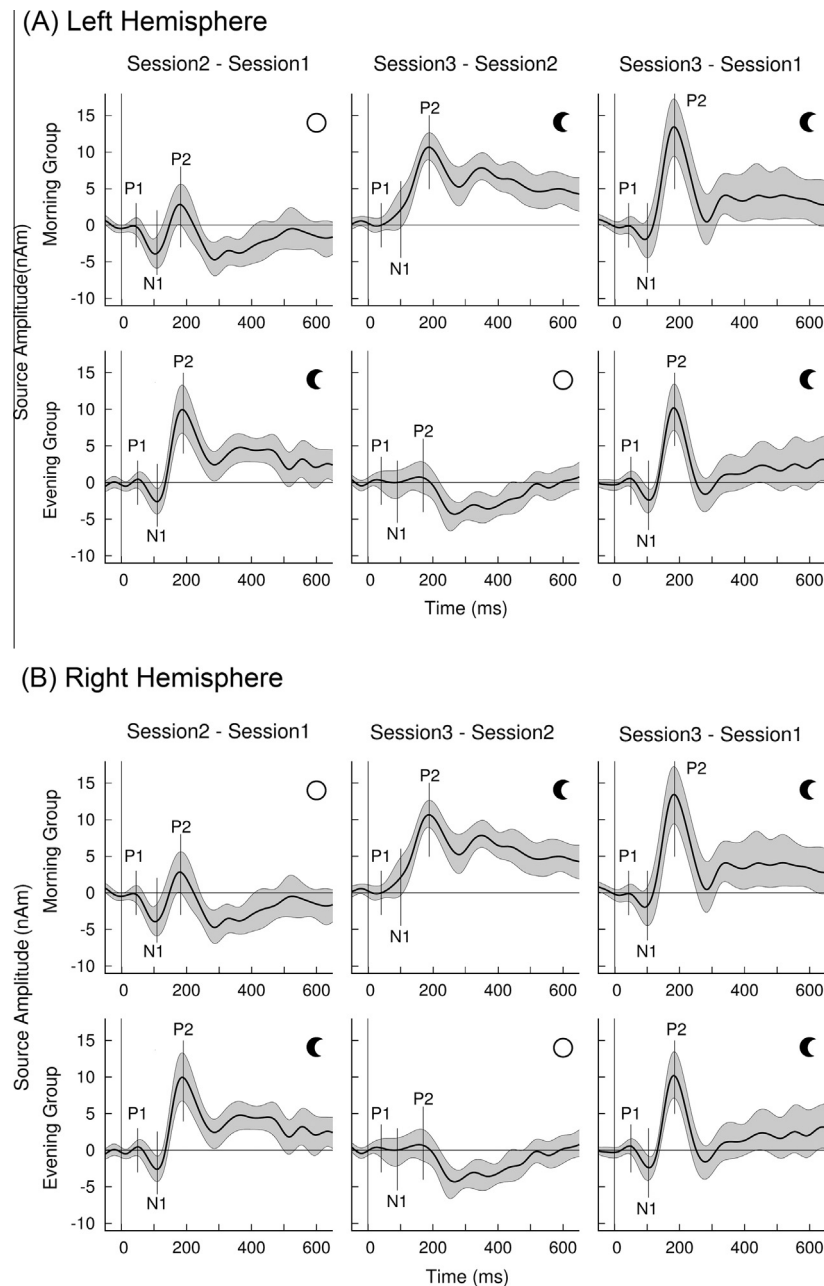


Fig. 6. Group mean difference in source waveforms (thick black line) between sessions and the 95% confidence limits (thin line) for the group mean estimate by bootstrap resampling. S2–S1 = session 2 minus session 1; S3–S2 = session 3 minus session 2; S3–S1 = session 3 minus session 1.

cal instrument played by the musicians (Shahin, Roberts, & Trainor, 2004). The source generator for the peak P2m response originates in or near Heschl's gyrus and is at least partially frequency dependent (Lütkenhöner & Steinstrater, 1998). Larger evoked potentials/fields in musicians may reflect a form of cortical remodeling associated with repeated exposure to musical sounds (Pantev & Lütkenhöner, 2000). There is also evidence to suggest that the P2 enhancement is not limited to musical training and has also been shown to be influenced by the familiarity of environmental sounds (Kirmse, Jacobsen, & Schroger, 2009). Together, these findings suggest that P2 may index sound object representations and that training and repeated exposure over several days can refine (i.e., enrich) these representations.

As participants were tested either in the early morning or late evening, TOD effects may have played a role in behavioral

improvements and neurophysiological changes. Converging evidence from both human and animal studies has shown that cognitive processing is affected by TOD. In general, task performance is impaired when testing occurs during sub-optimal (off-peak) periods of the day than testing during optimal (peak) periods (May, Hasher, & Foong, 2005; Winocur & Hasher, 2004). In the current study, it is unlikely that TOD preference affected the results. First, TOD preference did not differ between groups with the majority of participants being classified as "neutral." Second, subjective reports of alertness during each test session did not change as a function of TOD in either group. Third, subjective measures of sleep quality (over the previous month) and duration did not show group differences. The auditory evoked P2 response has been shown to be unrelated to both objective measures of sleep duration and efficiency among younger adults who reported no history of sleep dif-

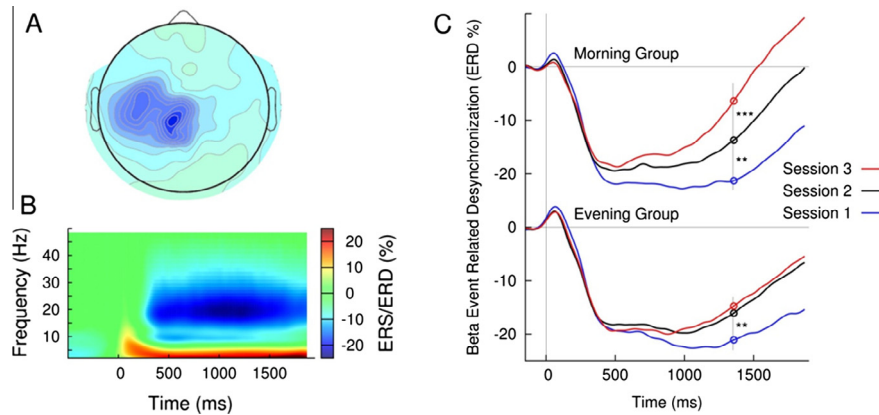


Fig. 7. Event-related changes in beta oscillations. A: Topographic map of signal power decrement at beta frequencies (18–25 Hz) in the latency interval 800–1200 ms. B: Time–frequency representation of the group mean MEG signal in a group of left central sensors. C: Group mean time courses of beta desynchronization for both experimental groups and the three sessions. Asterisks denote significant between-session differences in the 1200–1500 ms latency interval.

faculties (Turcotte & Bastien, 2009). Most importantly, the performance of the first test session was equivalent regardless of whether testing initially occurred in the morning or evening.

Changes in beta oscillations have been associated with demands in short-term memory (Leiberg et al., 2006) and as an indicator for learning in classical conditioning experiments (Moses, Bardouille, Brown, Ross, & McIntosh, 2010). In the present study, the observed changes in beta oscillations paralleled behavioral improvements in both groups. Modulation of beta oscillations was greater over left central areas, near the sensorimotor cortex. Given that participants generated their responses using their right hand, the change in beta may index motor learning associated with the task. The lesser expressed beta desynchronization indicated that less sensorimotor resources were required for the response. With practice, participants became better at remembering the stimulus–response mapping. Interestingly, the time course for this kind of motor learning differed from that observed for the P2m, which mainly manifested itself only after a night of sleep. Here, the changes in beta oscillations are more prominent between the first and second test sessions irrespective of sleep.

In summary, our data show that concurrent vowel segregation and identification improved with practice, which was accompanied by specific changes in neuromagnetic activity when learning occurred within the same day and between days. These changes in neuromagnetic activity likely reflect different stages of consolidation. These practice-related modulations in neuromagnetic activity may reflect intrinsic changes in the underlying neural generators, which could be expressed as: (1) an increase in the size of cortical areas representing the trained attribute; (2) higher degrees of synchronization within a particular neural ensemble; (3) a sharpening in the tuning of cells for the task-relevant (trained) attributes; and/or (4) changes in cortical maps representing the trained attribute. An alternative possibility to changes in the P2m generators is that training affects other processes that overlap these waves in time. For instance, the P2m wave may be superimposed by a slow negative wave associated with the goal-directed task. This may be similar to the processing negativity component used to account for the effects of attention on AEPs (Alho, Tottola, Reinikainen, Sams, & Naatanen, 1987; Hansen & Hillyard, 1980). The postulate is that all stimuli would elicit this processing negativity whose onset, duration, and/or amplitude would change with learning. As the listener becomes more familiar with the stimuli, the time or effort allocated to make a perceptual decision decreases. This would be reflected in the AEFs by a reduced superimposition of a goal-directed component on the P2m wave. From this perspective, the training-induced P2 enhancement would

occur because the P2 wave is less “contaminated” by other negative components. In other words, practice-related modulations in P2m waves could involve a genuine change in sensory discrimination abilities (i.e., sensory learning) or they could reflect the participant’s progressive adaptation to the cognitive demands of the task and test procedure (e.g., changes in attentional demands or task learning). The latter account is akin to the reverse hierarchical theory (Ahissar, Nahum, Nelken, & Hochstein, 2009), where learning first influence higher level of representation that eventually twinkles down to lower level of processing. Future research is needed to directly test the relationship between training-related changes in ERPs P2 and the transfer from higher to lower order representations in the auditory system.

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